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FILE COVERS 1907 - 6 Mar 2006 VOL 144 ISS 11

FILE LAST UPDATED: 5 Mar 2006 (20060305/ED)

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=> s 146-14-5/rn or 146-17-8/rn or 752-56-7/rn or 6155-39-1/rn or 13345-95-4/rn  
6005 146-14-5  
142 146-14-5D  
5884 146-14-5/RN  
(146-14-5 (NOTL) 146-14-5D )

3426 146-17-8  
 112 146-17-8D  
 3334 146-17-8/RN  
       (146-17-8 (NOTL) 146-17-8D )  
 242 752-56-7  
       1 752-56-7D  
 241 752-56-7/RN  
       (752-56-7 (NOTL) 752-56-7D )  
       3 6155-39-1  
       0 6155-39-1D  
       3 6155-39-1/RN  
       (6155-39-1 (NOTL) 6155-39-1D )  
       66 13345-95-4  
       2 13345-95-4D  
       64 13345-95-4/RN  
       (13345-95-4 (NOTL) 13345-95-4D )  
 L14 8253 146-14-5/RN OR 146-17-8/RN OR 752-56-7/RN OR 6155-39-1/RN OR  
       13345-95-4/RN

=> s l4 and (hypercytokinemia or lymphokine or cytokine)  
       18618 L4  
       65 HYPERCYTOKINEMIA  
       11555 LYMPHOKINE  
       91836 CYTOKINE  
 L15 7 L4 AND (HYPERCYTOKINEMIA OR LYMPHOKINE OR CYTOKINE)

=> s l14 and (hypercytokinemia or lymphokine or cytokine)  
       65 HYPERCYTOKINEMIA  
       11555 LYMPHOKINE  
       91836 CYTOKINE  
 L16 11 L14 AND (HYPERCYTOKINEMIA OR LYMPHOKINE OR CYTOKINE)

=> d 1-11 bib abs

L16 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:1054462 CAPLUS  
 DN 142:28174  
 TI Pharmaceutical compositions containing riboflavins and ubidecarenone,  
       preparations separately containing two components, use of them as  
       cytokine production inhibitors, and the inhibitors  
 IN Kodama, Kotaro; Araki, Seiichi; Toyosawa, Itsuo; Suzuki, Mamoru; Kimata,  
       Motoki; Tsujimoto, Michihiko  
 PA Eisai Co., Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 14 pp.  
       CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2004345988	A2	20041209	JP 2003-143179	20030521
PRAI	JP 2003-143179		20030521		
AB	Compsn. containing ≥1 selected from riboflavin, its derivs., or their pharmacol. acceptable salts and ≥1 selected from ubidecarenone, its derivs., and their pharmacol. acceptable salts are useful for treatment of hypercytokinemia in Alzheimer disease, rheumatoid arthritis, gout, septicemia, etc., and chronic inflammatory diseases such as dermatitis, mastitis, etc., alleviation of phys. fatigue, and activation of energy production. Thus, simultaneous addition of 5'-FMN-Na and CoQ10 to mouse peritoneal macrophage significantly inhibited LPS-induced IL-6 production				

L16 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:633950 CAPLUS  
 DN 141:169975  
 TI Purification, cloning and characterization of L-amino acid oxidase with

cytotoxic activity from Aplysia punctata and use for the diagnosis and treatment of cancer

IN Butzke, Daniel; Goedert, Sigrid; Dittrich, Michael; Rudel, Thomas; Meyer, Thomas F.

PA Max-Planck-Gesellschaft Zur Foerderung Der Wissenschaften E.V., Germany

SO PCT Int. Appl., 125 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004065415	A2	20040805	WO 2004-EP423	20040120
	WO 2004065415	A3	20050120		
	W:	AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI			
	EP 1585761	A2	20051019	EP 2004-703388	20040120
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRAI	EP 2003-1232	A	20030120		
	EP 2003-26613	A	20031119		
	WO 2004-EP423	W	20040120		

AB The present invention relates to a cytotoxic polypeptide which is an L-amino acid oxidase isolated from the ink of the sea hare Aplysia punctata via anion exchange chromatog. and gel filtration. The polypeptide is termed APIT (Aplysia punctata ink toxin). Tumor cells treated with APIT displays a morphol. which is neither typical for apoptosis nor for necrosis but rather is typical for oxidative damage induced cell death. The cDNA sequence and the encoded amino acid sequence of APIT isoforms are provided. The toxic and enzymic activity of APIT is due to the presence of an attached FAD. It was demonstrated that the cytotoxic activity depended on the H2O2 producing enzymic activity of APIT. From all amino acids tested only L-lysine and L-arginine served as substrates for APIT to produce hydrogen peroxide. Sensitivity of different tumor cell lines to APIT induced cell death was studied. Change in protein expression pattern in Jurkat T cells after treatment with APIT was investigated. The influence of APIT on the gene expression of tumor cells was investigated by Microarray technol. It was shown that healthy human cells are resistant against the APIT-induced cell death. APIT can be used for the manufacture of a medicament for the diagnosis and treatment of cancer.

L16 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:818294 CAPLUS

DN 139:297048

TI Drugs containing riboflavin compound

IN Araki, Seiichi; Suzuki, Mamoru; Kodama, Kohtarou; Toyosawa, Toshio

PA Eisai Co., Ltd., Japan

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003084545	A1	20031016	WO 2003-JP4511	20030409
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,			

PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,  
 TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003227475 A1 20031020 AU 2003-227475 20030409  
 PRAI JP 2002-106685 A 20020409  
 WO 2003-JP4511 W 20030409

AB Disclosed is a drug composition comprising at least one member selected from among riboflavin, a riboflavin derivative and a pharmacol. acceptable salt thereof, at least one member selected from among protein C, an activated protein C and derivs. of these, and/or valine as active ingredients and/or an immune activator or protective remedy of enhanced efficacy. An i.v. injection of Na riboflavin phosphate at 10 mg/kg and activated protein C 75 units/kg to endotoxin-induced shock model mice significantly increased the survival rate.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:737589 CAPLUS

DN 139:255348

TI Drugs containing riboflavin-type compounds

IN Araki, Seiichi; Suzuki, Mamoru; Kodama, Kohtarou; Toyosawa, Toshio

PA Eisai Co., Ltd., Japan

SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075935	A1	20030918	WO 2003-JP2868	20030311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003211586	A1	20030922	AU 2003-211586	20030311
EP 1484061	A1	20041208	EP 2003-744055	20030311
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005208124	A1	20050922	US 2005-506631	20050411
PRAI JP 2002-65720	A	20020311		
WO 2003-JP2868	W	20030311		

AB It is intended to provide drugs that contain as the active ingredient at least one member selected from among riboflavin, riboflavin derivs. and pharmacol. acceptable salts thereof and have an effect of inhibiting a cytokine such as IL-1 $\beta$ , IL-6, IL-10, INF- $\gamma$ , TNF- $\alpha$ , GM-CSF, IL-8 or MCP-1; and preventives or remedies that have an excellent cytokine inhibitory effect for inflammatory diseases accompanied by hypercytokinemia.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:684112 CAPLUS

DN 123:252728

TI Further characterization and comparison of inducible nitric oxide synthase

in mouse, rat, and human hepatocytes

AU Nussler, Andreas K.; Silvio, Mauricio Di; Liu, Zhi-Ze; Geller, David A.;  
Freeswick, Paul; Dorko, Kenneth; Bartoli, Fabio; Billiar, Timothy R.

CS Department Surgery, University Pittsburgh, Pittsburgh, PA, USA

SO Hepatology (Philadelphia) (1995), 21(6), 1552-60  
CODEN: HPTLTD9; ISSN: 0270-9139

PB Saunders

DT Journal

LA English

AB Marked differences in induced nitric oxide (NO) synthesis occur between species. The authors have previously shown that both human and rat hepatocytes express an inducible NO synthase in response to cytokines and lipopolysaccharide. In this study, the authors compare the expression and regulation of cytokine-induced NO synthase in hepatocytes isolated from three species, human, rat, and mouse. On stimulation with tumor necrosis factor alpha (TNF $\alpha$ ), interleukin-1 $\beta$  (IL-1 $\beta$ ), interferon gamma (IFN $\gamma$ ), and lipopolysaccharide (LPS), it was found that hepatocytes from all three species produce high levels of NO with levels of production exhibiting the following hierarchy: rat hepatocytes > mouse hepatocytes > human hepatocytes. Whereas rat and mouse hepatocytes express inducible NO synthase mRNA in response to TNF $\alpha$ , IL-1 $\beta$ , or IFN $\gamma$  as a single stimulus, human hepatocytes respond to LPS alone. Inhibition of NO generation through transforming growth factor (TGF- $\beta$ 1) was seen in mouse (77%) and rat hepatocytes (17%) whereas only about 10% was seen in human hepatocytes. Epidermal growth factor (EGF) was shown to inhibit NO synthesis in human and mouse hepatocytes but not rat. A marked NO-dependent inhibition of total protein synthesis was seen in rat and human hepatocytes, whereas mouse hepatocytes showed almost no inhibition in protein synthesis when stimulated. NO-dependent cGMP release was found in all three species. Comparative studies on cytosol for inducible NO synthase enzyme activity showed that mouse and rat hepatocyte cytosol needed only L-arginine and reduced form of nicotinamide-adenine dinucleotide phosphate (NADPH) to exhibit NO formation, whereas cytosol from human hepatocytes required the addition of 5,6,7,8-tetrahydrobiopterin, FMN, and FAD to exhibit maximal NO synthase activity. The results show even though hepatocytes from all three species can express considerable inducible NO synthase activity, important differences exist in the characteristics and effects of the NO synthesis.

L16 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:133502 CAPLUS

DN 122:49741

TI Cloning and functional expression of human inducible nitric oxide synthase (NOS) cDNA from a glioblastoma cell line A-172

AU Hokari, Atsushi; Zeniya, Mikio; Esumi, Hiroyasu

CS Biochemistry Division, National Cancer Center Research Inst., Tokyo, 104, Japan

SO Journal of Biochemistry (Tokyo, Japan) (1994), 116(3), 575-81  
CODEN: JOBIAO; ISSN: 0021-924X

DT Journal

LA English

AB Nitric oxide (NO) is a messenger mol. with diverse functions throughout the body. The inducible type of nitric oxide synthase (NOS) is considered to be a key mol. in the immune responses to bacteria, parasites, and tumors, and its gene expression is regulated by cytokines. The authors isolated 3 overlapping partial inducible NOS cDNA clones from a human glioblastoma cell line A-172 induced by IL-1, TNF- $\alpha$ , and IFN- $\gamma$ . The 3,963-bp human glioblastoma inducible NOS-cDNA contained the longest open reading frame of 3,450 bp, which encoded a polypeptide of 1,153 amino acids with a calculated mol. mass of 131 kDa. This human inducible NOS possessed consensus recognition sites for the cofactors FMN, FAD, and NADPH and calmodulin recognition sites, and displayed 48.1% sequence identity with the endothelial type, 43.1% with the neuronal type, an 99.3% with the inducible type from hepatocytes, and 99.9% with the

inducible type from chondrocytes and adenocarcinoma. An expression plasmid consisting of pSG5 expression vector and cDNA containing the entire putative encoding sequence was constructed and transfected into COS-1 cells. COS-1 cells showed nitric oxide synthase activity together with a 130 kDa immunoreactive band on Western blot anal.

L16 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:549114 CAPLUS

DN 121:149114

TI Method for using polynucleotides, oligonucleotides, and derivatives thereof to treat various disease states

IN Burcoglu, Arsinur

PA USA

SO PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9415621	A1	19940721	WO 1994-US638	19940113
	W: AU, CA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2153778	AA	19940721	CA 1994-2153778	19940113
	CA 2153778	C	20040706		
	AU 9460904	A1	19940815	AU 1994-60904	19940113
	AU 692433	B2	19980611		
	EP 678029	A1	19951025	EP 1994-907246	19940113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 2003013669	A1	20030116	US 2001-754066	20010105
	US 6699985	B2	20040302		
	US 2004138167	A1	20040715	US 2004-768089	20040202
PRAI	US 1993-2395	A2	19930113		
	US 1991-748277	B2	19910821		
	US 1991-815130	B2	19911227		
	US 1992-830886	B2	19920204		
	WO 1994-US638	W	19940113		
	US 1994-185416	A2	19940124		
	US 1997-848013	B1	19970428		
	US 2001-754066	A3	20010105		
AB	Oligodeoxyribonucleotides, polydeoxyribonucleotides, and derivs. thereof, e.g. defibrotide, are agents of genetic modulation at the levels of transcription, translation, secondary messengers, and cellular signal transduction systems. Various disease states can be treated by modifying the dose of such agents in response to observed fluctuations (e.g., increase, decrease, appearance, disappearance) in normal, disease and repair markers. The specificity of defibrotide for HIV virus in HIV-infected peripheral blood mononuclear cells was evaluated. Treatment of HIV-infected patients, as well as of patients with other diseases, is described.				

L16 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1993:554557 CAPLUS

DN 119:154557

TI Macrophage nitric oxide synthase subunits. Purification, characterization, and role of prosthetic groups and substrate in regulating their association into a dimeric enzyme

AU Baek, Kwang Jin; Thiel, Bonnie A.; Lucas, Shawn; Stuehr, Dennis J.

CS Dep. Immunol., Cleveland Clin., Cleveland, OH, 44195, USA

SO Journal of Biological Chemistry (1993), 268(28), 21120-9

CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB The cytokine-induced nitric oxide synthase (NOS) of macrophages is a homodimeric enzyme that contains iron protoporphyrin IX (heme), FAD,

FMN, tetrahydrobiopterin, and calmodulin. To investigate how the enzyme's quaternary structure relates to its catalytic activity and binding of prosthetic groups, dimeric NOS and its subunits were purified sep. and their composition and catalytic properties compared. In contrast to dimeric NOS, purified subunits did not synthesize NO or contain bound heme or tetrahydrobiopterin. However, the subunits did contain FAD, FMN, and calmodulin in amts. comparable with dimeric NOS, displayed the light absorbance spectrum of an FAD- and FMN-containing flavoprotein, and generated an air-stable flavin semiquinone radical upon reduction of their ferricyanide-oxidized form. Dimeric NOS and NOS subunits were equivalent in catalyzing electron transfer from NADPH to cytochrome c, dichlorophenolindophenol, or ferricyanide at rates that were 8-30-fold faster than the maximal rate of NO synthesis by dimeric NOS. Reconstitution of subunit NO synthesis required their incubation with L-arginine, tetrahydrobiopterin, and stoichiometric amts. of heme and correlated with formation of a proportional amount of dimeric NOS in all cases. The dimeric NOS reconstituted from its subunits contained 0.9 heme and 0.44 tetrahydrobiopterin bound per subunit and had the spectral and catalytic properties of native dimeric NOS. Thus, NOS subunits are NADPH-dependent reductases that acquire the capacity to synthesize NO only through their dimerization and binding of heme and tetrahydrobiopterin. The ability of heme, tetrahydrobiopterin, and L-arginine to promote subunit dimerization is unprecedented and suggests novel roles for these mols. in forming and stabilizing the active dimeric NOS.

- L16 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 1993:228720 CAPLUS  
 DN 118:228720  
 TI The cytokine-induced macrophage nitric oxide synthase is a flavoprotein containing flavin adenine dinucleotide and flavin mononucleotide  
 AU Stuehr, D. J.; Cho, H. J.; Kwon, N. S.; Nathan, C. F.  
 CS Cleveland Clin., Cleveland, OH, 44195, USA  
 SO Biol. Nitric Oxide, Proc. Int. Meet., 2nd (1992), Meeting Date 1991, Volume 2, 1-3. Editor(s): Moncada, Salvador. Publisher: Portland Press, London, UK.  
 CODEN: 59AFA7  
 DT Conference; General Review  
 LA English  
 AB A review with 13 refs. on evidence indicating that cytokine-induced macrophage nitric oxide synthase is a flavoprotein containing FAD and FMN. Some implications of this with regard to the enzyme reaction mechanism are discussed.
- L16 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 1992:166702 CAPLUS  
 DN 116:166702  
 TI Human fat cells possess a plasma membrane-bound hydrogen peroxide generating system that is activated by insulin via a mechanism bypassing the receptor kinase  
 AU Krieger-Brauer, Heidemarie I.; Kather, Horst  
 CS Klin. Inst. Herzinfarktforsch., Med. Universitaetsklin., Heidelberg, D-6900, Germany  
 SO Journal of Clinical Investigation (1992), 89(3), 1006-13  
 CODEN: JCINAO; ISSN: 0021-9738  
 DT Journal  
 LA English  
 AB Insulin caused a transient increase in H<sub>2</sub>O<sub>2</sub> accumulation in human fat cell suspensions that was observed only in the presence of an inhibitor of catalase and heme-containing peroxidases, such as azide, and reached peak levels of 30  $\mu$ M within 5 min. The cells contained a plasma membrane-bound NADPH oxidase, producing 1 mol H<sub>2</sub>O<sub>2</sub>/mol of NADPH oxidation, that was activated on exposure of intact cells to insulin at concns. that are physiol. relevant (0.1-10 nM). The hormone effect was rapid and was due to a selective increase in substrate affinity. The enzyme was

magnesium dependent, required a flavin nucleotide for optimal activity, and was most active at pH 5.0-6.5. In contrast to all other hormone- or cytokine-sensitive NADPH oxidases that have been characterized in sufficient detail, the human fat cell oxidase retained its hormone responsiveness after cell disruption, and only Mn<sup>2+</sup>, but no ATP, was required for a ligand-induced activation in crude plasma membranes. The results demonstrate that insulin utilizes tyrosine kinase-independent pathways for receptor signaling and strongly support the view that H<sub>2</sub>O<sub>2</sub> contributes to the intracellular propagation of the insulin signal.

L16 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1991:577948 CAPLUS  
DN 115:177948  
TI Purification and characterization of the cytokine-induced  
macrophage nitric oxide synthase: an FAD- and FMN-containing flavoprotein  
AU Stuehr, Dennis J.; Cho, Hearn J.; Kwon, Nyoun Soo; Weise, Mary F.; Nathan,  
Carl F.  
CS Med. Coll., Cornell Univ., New York, NY, 10021, USA  
SO Proceedings of the National Academy of Sciences of the United States of  
America (1991), 88(17), 7773-7  
CODEN: PNASA6; ISSN: 0027-8424  
DT Journal  
LA English  
AB A soluble nitric oxide (NO) synthase activity was purified 426-fold from a  
mouse macrophage cell line activated with interferon  $\gamma$  and bacterial  
lipopolysaccharide by sequential anion-exchange, affinity, and gel  
filtration chromatog. SDS/PAGE of the purified NO synthase gave three  
closely spaced silver-staining protein bands between 125 and 135 kDa.  
When assayed in the presence of L-arginine, NADPH, tetrahydrobiopterin,  
FAD, and reduced thiol, purified NO synthase had a specific activity of  
1313 nmol of NO<sub>2</sub><sup>-</sup> plus NO<sub>3</sub><sup>-</sup> per min per mg. The apparent K<sub>m</sub> of the enzyme  
for L-arginine and NADPH was 2.8 and 0.3  $\mu$ M, resp. Addition of calcium  
ions with or without calmodulin did not increase the activity of the  
purified enzyme, and NO synthesis was not altered by calmodulin  
inhibitors. Gel filtration chromatog. indicated that the induced NO  
synthase was catalytically competent as a dimer of  $\approx$ 250 kDa but  
could be dissociated into inactive monomers of  $\approx$ 130 kDa in the  
absence of L-arginine, FAD, and tetrahydrobiopterin. Upon heat  
denaturation, NO synthase released 1.1 mol of FAD and 0.55 mol of FMN per  
mol of 130-kDa subunit. Thus, inducible macrophage NO synthase differs in  
several respects from constitutive NO synthases and is one of very few  
eukaryotic enzymes containing both FAD and FMN.

=>

---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	63.18	212.24
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-8.25	-13.50

STN INTERNATIONAL LOGOFF AT 19:43:33 ON 06 MAR 2006